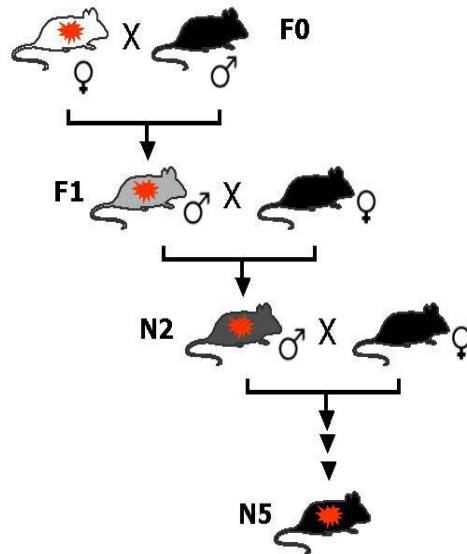


LASP “Speed Congenics” Services: Accelerated Derivation of Congenic Mouse Strains Using Marker-Assisted Breeding

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Congenic strains are developed by repeated backcross breedings of a donor strain (depicted as a white mouse) carrying a mutation or genetic region of interest (red star) to an inbred recipient strain (black mouse). In traditional backcrosses it would take 10-12 generations until 99.9% of the genetic background of the progeny is of recipient origin while still retaining heterozygosity at the region of interest (Snell 1948). The recent availability of dense genetic maps of the mouse genome has allowed the development of marker-assisted breeding strategies that aim to reduce the number of generations required to eliminate donor strain-derived alleles outside the genetic region of interest (Markel et al. 1997).



Using marker-based selection for genetically optimal breeders at each generation >99.9% recipient strain genome content can be reached after five backcrosses (generation N5). The time frame for derivation of a “speed congenic” strain, assuming no problems with breeding or health, etc. will be approximately 98 days per generation or 1.3 years to complete the project, as opposed to 2.5 years for a conventional congenic.

When beginning a “speed congenic” project, ideally 2-3 female mice carrying the genetic region of interest are outcrossed to a male of the recipient strain to assure that all males of the F1 generation will carry the Y chromosome from the recipient strain. Two to three male F1 animals carrying the genetic region of interest are then backcrossed to recipient-strain females to produce N2 progeny. Note that due to this breeding scheme all N2 males will carry both sex chromosomes from the recipient strain.

Genetic selection begins at the N2 generation. Approximately 20 male mice are genotyped to identify carriers of the mutation or genetic region of interest. Ten of these are then subjected to autosomal genome scans using 96 microsatellite markers that are polymorphic between the donor and recipient strains. Two to four males with the highest percentage of recipient strain contribution are selected as breeders for the next backcross.

This process of marker-assisted selection and breeding is repeated at each generation out to N5. At this point, male and female mice with >99.9% recipient genome content can be intercrossed to produce homozygous congenics.

The LASP speed congenics services at NCI-Frederick may be requested through the “Yellow Task” system (URL: http://web.ncifcrf.gov/rtp/lasp/yellow_task.asp). This web-based interface enables investigators to obtain cost and time estimates for each project. NCI approval is an integral function of this process, which ensures that adequate funding and other resources are available to perform the work.

For more information please contact Dr. Dieter Naf at 301-846-7132 or dnaf@ncifcrf.gov

References:

Markel P, Shu P, Ebeling C, Carlson GA, Nagle DL, Smutko JS, Moore KJ (1997). Theoretical and empirical issues for marker-assisted breeding of congenic mouse strains. *Nature Genetics* 17, 280-284.

Snell GD (1948). Methods for the study of histocompatibility genes. *Journal of Genetics* 49, 87-108.